REMARKS

In view of the amendments to the claims and the following remarks, the Examiner is requested to allow claims 34, 45-52, 61, 62, 69, 77, 79 and new claim 81, the only claims pending and under examination in this application.

FORMAL MATTERS:

Claim 69 has been amended for clarity. Specifically, the recitation of "wherein said endogenous GPCR comprises a mutation in its amino acid sequence so as to render it constitutively active" has been replaced with "obtaining a constitutively activated form of said endogenous GPCR, wherein said constitutively activated GPCR comprises a mutation in its amino acid sequence that increases its constitutive activity relative to said endogenous GPCR". Claim 69 has also been amended to change the word "determining" to "analyzing".

Claim 77 has been amended to recite "obtaining a constitutively activated form of said endogenous orphan GPCR, wherein said constitutively activated GPCR comprises a mutation in its amino acid sequence that increases its constitutive activity relative to the endogenous orphan GPCR" (similar to Claim 69), thereby incorporating the subject matter of Claim 80. Claim 77 has also been amended to replace the word "comparing" in (c) with "analyzing" as well as to be consistent with the "obtaining" step amendment. Support for these amendments can be found throughout the specification, e.g., on page 5, lines 10-14 and lines 27-30; page 31, line 22 to page 32 line 4; and page 35 lines 19-21.

Claim 80 has been canceled in view of the amendment to Claim 77.

Claims 45, 52 and 79 have been amended to be consistent with the amendments to Claims 69 and 77.

Claim 81 is added and specifies that the claimed method "is performed in a laboratory or research setting". Support for this claim can be found throughout the specification, see, e.g., page 55, lines 2-12 (and continuing through to page 58); and page 63, lines 14-22. In addition, the experiments in the Examples all are "performed in a laboratory or research setting."

As no new matter is added by these amendments, entry by the Examiner is respectfully requested.

GRANTED CLAIMS IN CORRESPONDING EUROPEAN PATENT:

Applicants provide herewith a copy of claims that have been granted in the European counterpart to the subject application (Exhibit A). The granting of these claims, which mirror those in the subject application, indicates that the European Patent Office considers them to have clear industrial applications (i.e., to have utility).

INTERVIEW REQUEST:

Prior to filing the present Amendment and Response, Applicants requested an interview to discuss the outstanding utility rejection. However, the Examiner indicated that he and his supervisor considered that further discussion of the utility rejection would not be productive because they considered that the arguments supporting and rejecting utility of the claimed invention had been fully exhausted. Applicants are aware that prosecution of the present application has been long and that the utility issue has been difficult to resolve. However, Applicants consider that the issue of the utility of the claimed invention is one that has been constantly evolving and possibly nearing resolution.

Therefore, Applicants respectfully request that the Examiner, after review of the present amendment and response, reconsider extending the courtesy of an interview to discuss any remaining issue that is preventing allowance of the presently claimed invention.

REJECTIONS UNDER §101, UTILITY

Claims 34, 40, 45-66, 69 and 70 stand rejected under 35 U.S.C. §101 as lacking patentable utility.

In maintaining this rejection, the Office Action asserts that the claimed invention fails to meet the utility requirement because "the claimed methods lack a specific and substantial utility because there is no specific and substantial utility for a non-endogenous modulatory compound identified by the claimed method" (page 4).

The Office Action further cites MPEP §2107, which states that: "Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities... the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities": (A) Basic research such as studying the properties of the claimed product

itself or the mechanisms in which the material is involved; (B) A method of treating an unspecified disease or condition; **(C) A method of assaying for or identifying a material that itself has no specific and/or substantial utility**" (emphasis added).

It appears to Applicants that item (C) above is being applied to the subject invention. Applicants respectfully traverse.

First, Applicants submit that the claimed invention is not drawn to "assaying for or identifying a material" as stated in item (C) above. Applicants submit that methods of "assaying **for** or identifying **a** material" (*emphasis added*) are those assays which merely detect the presence or absence of an analyte in a sample (and in the MPEP Guidance, the analyte itself would have no utility). This MPEP Guidance **is not** directed towards Applicants claimed invention. Specifically, Applicants submit that the phrase "assaying for or identifying a material" does not contemplate screening assays that analyze the functional activity of a compound as currently claimed. In the subject application, a plurality of candidate compounds are screened to find compounds that can modulate a particular orphan GPCR. This assay does not merely assay for or identify a material in a sample.

Thus, Applicants submit that, at least in one embodiment of the claimed invention, a different section of MPEP 2107 is applicable. Specifically, MPEP 2107.01(C), under the heading "Research Tools", states the following:

> C. Research Tools
> Some confusion can result when one attempts to label certain types of inventions as not being capable of having a specific and substantial utility based on the setting in which the invention is to be used. One example is inventions to be used in a research or laboratory setting. Many research tools such as gas chromatographs, **screening assays**, and nucleotide sequencing techniques have a clear, specific and unquestionable utility (e.g., they are useful in analyzing compounds).
> *(emphasis added)*

As explicitly stated above, research tools that are used in a research or laboratory setting, ***including screening assays as claimed in the present invention***, have "a clear, specific and unquestionable utility." In the case of the subject invention, the screening assay method identifies compounds that have modulatory activity on an orphan GPCR of interest. In one embodiment, these compounds can be employed in a predictable manner as reagents that have a known effect on the orphan GPCR (i.e., as agonists of inverse agonists).

Just as with sequencing assays, or, as argued previously, PCR assays, the user of the claimed screening assay determines which specific entity is the subject of the analysis (i.e., which specific orphan GPCR is to be employed to identify modulatory compounds). The reasons why a user wants to screen for modulatory compounds for a particular orphan GPCR will vary, including its activity in a specific cellular process (e.g., a disease process, like viral entry) as well as having an expression pattern of particular interest (e.g., in a specific diseased tissue or cells at a specific developmental stage). However, regardless of why a user is interested in a particular orphan GPCR, Applicants submit that the MPEP citation above clearly and explicitly states that screening assays have "a clear, specific and unquestionable utility."

Therefore, in view of the fact that the claimed screening assay is explicitly called out in MPEP 2107.01(C) as having "a clear, specific and unquestionable utility", Applicants submit that the claimed invention meets the utility requirements of 35 U.S.C. §101.

On page 6, the Office Action states that "the claims are rejected because they are directed solely to a method of identifying compounds for which there is no specific and substantial utility once identified. This is because the compounds modulate the activity of uncharacterized orphan receptors and this activity has not been associated with any particular, immediate use."

First, Applicants submit that a person skilled in the art would not make the effort to screen an orphan GPCR if they did not have some use for the compounds identified by the screening method. As detailed above, Applicants contend that the claimed screening assay has a specific and substantial "real world" use because it allows a user to identify, from a library of candidates, specific compounds that have a defined modulatory activity for an orphan GPCR of interest, regardless of the reason for why it is of interest to a user. This utility is clearly described throughout the application as providing researchers in the field with a novel approach to by-pass the significant bottle-neck in the orphan GPCR field, i.e., waiting for an orphan GPCR to be "de-orphanized" prior to conducting further functional studies. In view of this, Applicants submit that those of ordinary skill in the art would consider the claimed invention to have a particular and immediate use.

Second, Applicants contend that prior to the time of filing the present application, orphan GPCRs having a specific function or activity had been identified, and that modulatory compounds for such an orphan GPCR do indeed have specific and substantial utility. Fr example, Applicants have previously

submitted references which disclose orphan receptors STRL33, gpr1 and gpr15 as co-factors for retroviral entry into cells (see response dated November 13, 2007, and exhibits filed therewith).

Applicants submit that it is a common misperception that orphan receptors, and by extension compounds that modulate orphan receptors, have no utility. Knowledge of a GPCR's natural ligand is simply not necessary for establishing a useful function for such a receptor. In fact, it is possible to know a receptor's function and develop and market pharmaceutical agents targeting it without any understanding of the natural ligand which activates it. For example, many opiates were identified and developed and the analgesic functionality of these compounds at the mu-opiate receptor was appreciated long before the first endogenous agonists of that receptor were discovered in 1975 (see Zadina et al., Ann NY Acad Sci. 1999; 897:136-44, provided herewith as Exhibit B for the Examiner's convenience).

Therefore, because orphan GPCRs have been characterized, even in the absence of a known endogenous ligand, Applicants submit that identifying modulatory compounds for such functionally-characterized orphan GPCRs represents a specific, substantial "real world" use of the claimed invention.

On page 8, the Office Action asserts that "[t]here is no specific and substantial utility for any of the non-endogenous compounds identified by the claimed methods. Further research would be required to identify a use for any of the modulators identified by the claimed methods."

While not conceding this point, Applicants again stress that the claimed invention is **not** drawn to compositions of compounds but rather to screening assays for identifying modulatory compounds for an orphan GPCR of interest to a user. The question with regard to the utility of the claimed invention is thus whether practicing the subject methods provides a specific and substantial "real world" use. Applicants contend that it does.

In making this rejection, the Office Action essentially is asserting that more research is needed to identify a specific and substantial use for the compounds identified in the claimed screening method. Applicants disagree. Again, the subject claims are drawn to screening assays for identifying a compound having a specific activity, i.e., having a modulatory activity for an orphan receptor of interest to the user. Such compounds have as much immediate utility as would the endogenous ligand for the receptor. Specifically, as with the endogenous ligand, the compounds identified in the claimed screening assay can be employed in a predictable manner as reagents that have a known effect on the orphan GPCR (e.g., as agonists or inverse agonists). While performing further experiments on these

compound may be done (e.g., to identify a therapeutic application for one or more of the identified compounds) this is not required for the claimed screening methods to have utility.

Finally, in the paragraph spanning pages 8 and 9, the Office Action states that Applicants arguments likening the utility of the claims of US Patent 5,462,856 with the claimed invention were not persuasive because, unlike the '856 patent, "the claimed method is not directed to GPCRs in general, but is instead limited to orphan GPCRs that have no known ligand and which have no known activity that can be modulated for a useful purpose." The Office Action also notes that, regardless of Applicants arguments, the '856 patent was issued prior to publication of the revised Utility Examination Guidelines of 1/5/01 in the Federal Register.

First, Applicants submit that, in contrast to the assertion in the Office Action, orphan GPCRs have indeed been identified that have a known activity, e.g., the mu-opiate receptor discussed above.

Second, Applicants note that the '856 patent was issued ***after*** publication of the revised Utility Examination Guidelines of 1/5/01 (the '856 patent issued on 10/31/05).

Based on the discussion above, Applicants respectfully submit that the claimed invention has a significant and presently available useful benefit to the public. Applicants thus respectfully request withdrawal of this rejection under 35 U.S.C. §101.

REJECTIONS UNDER §112, ¶1 (ENABLEMENT)

Claims 34, 40 and 45-66, 69 and 70 stand rejected as not meeting the "how to use" part of the enablement requirement of 35 U.S.C. § 112, first paragraph.

The basis for this rejection is the Examiner's contention that the claims are not supported by a patentable utility.

As such, it is believed that this rejection has been adequately addressed in the discussion in the preceding section of this response.

In view of the discussion in the preceding section of this response, Applicants respectfully request withdrawal of this rejection.

REJECTIONS UNDER §102(b)

Claims 34, 45, 48, 61, 77 and 79 stand rejected under 35 U.S.C. 102(b) as being anticipated by Eggerickx et al (Biochem J. 309(Pt. 3): 837-843).

It will be appreciated that the standard for anticipation under section 102 is one of strict identity. An anticipation rejection requires a showing that each limitation of a claim be found in a single reference, *Atlas Powder Co. v. E.I. DuPont de Nemours & Co.,* 224 U.S.P.Q. 409, 411 (Fed. Cir. 1984). Further, an anticipatory reference must be enabling, see *Akzo N.V. v. United States Int'l Trade Comm'n* 808 F.2d 1471, 1479, 1 U.S.P.Q.2d 1241, 1245 (Fed. Cir. 1986), *cert denied*, 482 U.S. 909 (1987), so as to place one of ordinary skill in possession of the claimed invention. To anticipate a claim, a prior art reference must disclose every feature of the claimed invention, either explicitly or inherently. *Glaxo v. Novopharm, Ltd.* 334 U.S. P.Q.2d 1565 (Fed. Cir. 1995).

Claims 34, 45, 48, 61 and 79 depend from independent Claim 77. Applicants note that Claim 80, which also depends from Claim 77, was not rejected as anticipated by the Examiner over Eggerickx et al.

Applicants have thus amended Claim 77 to include the subject matter of Claim 80. Specifically, Claims 77 recites "obtaining a constitutively activated form of said endogenous orphan GPCR, wherein said constitutively activated GPCR comprises a mutation in its amino acid sequence that increases its constitutive activity relative to the endogenous orphan GPCR".

Because Eggerickx et al. fails to teach this element of amended Claim 77, Applicants submit that this reference cannot anticipate it or its dependents. Applicants respectfully request withdrawal of this rejection.

CONCLUSION

Applicants submit that the pending claims are in condition for Allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, he is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order numberAREN-001CIP.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: June 26, 2009

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Enclosures:

1. Exhibit A: Copy of claims granted in European counterpart (8 pages);
2. Exhibit B: Zadina et al., Ann NY Acad Sci. 1999; 897:136-44 (9 pages)

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